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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/527,831	NORTH, KATHRYN NANCE	
	Examiner	Art Unit	
	Steven C. Pohnert	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16,18 and 24-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16,18 and 24-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 March 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/8/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This action is in response to papers filed 11/08/2007.

The deletion of the hyperlinks for Table 3 has overcome the objection to the drawings.

Deletion of hyperlinks from the specification has overcome the objection to the specification due to hyperlinks.

The objection to paragraph 27 has been overcome by amending the paragraph to refer to Table 6 for ethnic differences.

The 112-1st paragraph enablement and written description rejection have been modified in light of the arguments to reflect the scope of the pending claims.

The 103 rejections have been withdrawn in view of the argument that the examiner incorrectly interpreted teachings North to suggest that ACTN3 played a role in loss of type 2 fibers.

Maintained rejections

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-18 and 24-40 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of determining sprint,

strength, or power performance in human males comprising: obtaining a sample from a human male, analyzing the sample for the presence of the human ACTN3 577RR genotype, wherein the presence of the homozygous ACTN3 577RR genotype indicates an improved sprint, strength or power performance in a human male does not reasonably provide enablement for predicting sprint performance, endurance performance, power performance, or strength performance in "any" male or "any" female in any mammalian species by the detection any variation in the ACTN3 gene or presence of ACTN3 577RX, or 577XX genotype. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. These factors have been described by the court in re Wands, 8 USPQ2d 1400 (CA FC 1988). Wands states at page 1404,

"Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in the Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention and the breadth of the claims:

The claims encompass predicting athletic performance in "any" mammal based on the presence of one or more variation in ACTN3. "Any" mammal broadly encompasses dog, horse, camel, as exemplified in claim 3, as well as cats, mice, dolphins, whales etc.

The claims encompass the detection of "any" genetic variation "any" ACTN3 gene.

The claims encompass the detection of one or more variations in "any" ACTN3 gene of "any" mammal.

Claims 6 and 7 encompass detection of the presence of "any" 577R or 577RR alleles positively associated with sprinting or power performance.

Claim 8 encompass "any" 577XX being negatively associated with power performance.

Claim 9 encompasses the detection of "any" 577XX being positively associated with endurance performance.

Claim 4 encompasses the detection of "any" 1747C>T polymorphism of ACTN3 also known as R577X allele

Claim 18 draws the claims to the detection of at least one other gene.

Claim 40 encompasses selecting a mammals training program based on the presence of one or more genetic variation.

The amount of direction or guidance and the Presence and absence of working examples.

The specification teaches a study of Caucasian controls and elite athletes comprising 108 endurance and 83 endurance athletes, 88 African Zulu and 152 Australian Caucasian individuals, that elite sprint athletes had a lower frequency of the 577XX genotype of ACTN3 (6% versus 18% in Caucasian population, $p<0.05$)(see paragraph 100 and 102). Thus the specification teaches that elite sprint athletes were less likely to have the 577XX allele than the controls. Thus the specification teaches trained elite sprint athletes are more likely to have the 577RR genotype than untrained. It is noted that the elite sprint group is a group that has been selected by performance and thus may not be representative of the population as a whole.

The specification further teaches in 46 track athletes competing in events of 800m, 42 swimmers competing in events of 200 m, 9 judo athletes, 7 short-distance track cyclists, and 3 speed skaters. For comparison, a subset of 194 subjects (122 male and 72 female) classified independently as specialist endurance athletes and analyzed, including 77 long-distance cyclists, 77 rowers, 18 swimmers competing over distances of 400 m, 15 track athletes competing in events of 5,000 m, and 7 cross-country skiers. Thirty-two sprint athletes (25 male and 7 female) and 18 endurance athletes (12 male and 6 female) had competed at the Olympic level (paragraph 0103). The specification further teaches "genotypic profiles of the three control groups (150 blood donors, 71 healthy children, and 215 healthy adults) did not differ significantly from one another ($x^2=0.19$; $P=0.996$) nor from a previously genotyped group of 107 white Europeans" (paragraph 104).

The specification further teaches there was no significant genotype difference between the elite athletes and control (paragraph 105), although a strong association was seen in sprint athletes relative to controls ($x^2_{[df=5]}=23$; $P<0.001$) (see paragraph 105). The significant allele frequency differences were seen between sprint athletes and controls for both males ($x^2_{[df=1]}=14.8$; $P<0.001$) and females ($x^2_{[df=1]}=7.2$; $P<0.01$) (see paragraph 105). Further the specification teaches that the allele frequencies deviated significantly in opposite directions in the sprint and endurance athletes (both males ($x^2_{[df=1]}=13.3$; $P<0.001$) and females ($x^2_{[df=1]}=5.8$; $P<0.05$) (see paragraph 105). The specification teaches there were allelic difference between the trained elite athletes and controls. However, as the trained elite athletes have undergone a selection process based on performance and training it is unpredictable that the correlation are the only factor in athletic performance.

In example 3 the specification teaches that there is a trend toward significance of the 577XX genotype in endurance athletes, although this reaches statistical significance only in females (see paragraph 110).

In summary the specification teaches that there is no significant difference between elite athletes and controls, although there was a difference in sprint athletes, both male and female. Further the specification teaches there was a significant allele frequency difference between elite endurance athletes and elite sprint athletes.

The specification does not teach any other ACTN3 allele is associated with improved performance. The specification does not teach the R577X allele occurs in any

other species. The specification does not teach that any ACTN3 allele is predictive of athletic performance in any non-human mammal.

The state of prior art and the predictability or unpredictability of the art:

The prior art teaches the ACTN3 577X mutation has arisen in humans following the evolution of the ACTN3 gene from primates (Mills et al (Human Molecular Genetics (2001) Volume 10, pages 1335-1346) (see abstract). Mills teaches that ACTN3 is a homolog of ACTN2 (see abstract). Mills teaches there are four different ACTN homologs in mice and humans. Mills further teaches that the mouse ACTN3 may not be functionally redundant with the human ACTN3 (see page 1340, 2nd column, 1st full paragraph). Mills teaches that unlike humans and primates, ACTN2 is expressed in many fibers that do not express ACTN3, thus suggesting different regulation and/or function in mouse muscle fibers (see page 1339, 1st column). Mills further teaches ACTN3 homologs have not been isolated in other mammals (see page 1340, 2nd column, last paragraph). Mills teaches the ACTN3 577X allele has resulted due to a single mutation after the divergence of humans and chimpanzees from other mammals (see page 1340, 1st column, last 3 lines). Mills thus teaches that neither the 577X allele nor the ACTN3 gene is predictably found in "any" mammal.

Gene card (genecards.org/cgi-bin/carddisp.pl?gene=ACTN3&search=actn3&suff=txt, pages 1-11, 3/24/2007) teaches ACTN3 homologs have only been found in dog, fruitfly, zebrafish, mouse, chimpanzee, and rat (see page 11), while listing 32 species in which a homolog of ACTN3 has not been found. Genecard teaches there are 16,406 bases in the ACTN3 gene. Genecard

further teaches there are 9 known SNPs in the human ACTN3 gene and 33 cDNAs. Genecard thus teaches ACTN3 is not predictably present in all species.

O'Brein et al (Science magazine (1999) volume 286, pages 458-481) teaches there are between 4600 and 4800 mammalian species (see page 458, 1st column 2nd paragraph).

Brenner et al (Trends in Genetics (2001) volume 17, pages 414-418) teaches that, "Here, the 'homology-implies-equivalency' assumption is restricted to a subset of homologs that diverged in the most-recent common ancestor of the species sharing the homologs. This strategy is useful, of course. But it is likely to be far less general than is widely thought. Two species living in the same space, almost by axiom, cannot have identical strategies for survival. This, in turn, implies that two orthologous proteins might not contribute to fitness in exactly the same way in two species" (see page 414, 3rd column last full paragraph). Brenner specifically describes that although the leptin gene homologs have been found in mice and humans, their affect is different (see page 414, 3rd column last paragraph-3rd column page 415). Brenner specifically teaches that the leptin gene in mice plays a major role in obesity, but no such effect has been demonstrated in humans due perhaps to the different evolutionary forces. Brenner thus teaches that the activity and function of genes in different species is unpredictable.

Post filing art teaches that the frequencies of the R577X alleles in elite distance runners from Ethiopia and Kenya did not significantly differ from those of their respective control population (see Yang, et al (Med. Sci. Sport and Exercise (2005)

volume 37, s42). Yang et al further teaches, "this polymorphism does not contribute significantly to the phenomenal success of elite East African endurance runners."

Moran et al (European Journal of Human Genetics (2007) volume 15, pages 88-93) teaches in a study of 992 adolescent Greeks the presence of the 577R allele resulted in a significant association with sprint times over 40m in males, but not females (see abstract and table 1). However, Moran did not find any other significant correlation of the 577R with tests of power including handgrip strength, basketball throw, vertical jump or agility run (see table 1). Moran further tested aerobic capacity or VO2 max (commonly used tests of endurance performance) and did not see a significant relationship with the 577X allele (see table 1). Moran et al further teaches, "We found no evidence that the R577X genotype is associated with endurance or obesity related genotypes" (see page 93, 1st column last paragraph). Moran thus teaches the 577R allele is only predictably associated with sprint speed in males. Moran further teaches that the 577R allele is not predictably associated with any other power testing performed. Moran further teaches that the 577X allele is not predictably associated with endurance performance.

Lucia et al studied the frequency of the ACTN3 genotype in a group of 50 top level professional cyclists and 52 Olympic class endurance runners (International Journal of Sports Medicine(2006) volume 27, pages 880-884). Lucia study demonstrated there was no significant differences between the elite runners and cyclists and the R577X genotype. Thus Lucia teaches it would be unpredictable to associate the R577X genotype with improved endurance performance.

Pitsiladis et al (Lancet (2005) volume 366, pages s16-s17) teaches, "Although ACTN3 is an interesting candidate gene of physical performance, the use of a genetic test for this one gene to assess potential for athletic success cannot be justified given the multifactorial nature of sporting performance. Others have been persuaded to consider multiple genes when examining multifactorial traits such as physical performance. A professional Australian Rugby team called the Sea-Eagles has, for example, admitted genotyping 18 of their 24 players for 11 exercise-related genes and tailoring exercise training for the individuals on the basis of their results. Although some genes do affect the interindividual variation in physical performance and trainability, this knowledge cannot be used to predict sporting talent or to prepare a training schedule. The current genetic evidence does not warrant genotyping an individual to establish their ability to run fast when this trait can be measured far more effectively with a stopwatch." Thus Pitsiladis suggests genotyping to determine athletic performance is unpredictable.

The art teaches that presence of SNPs in the same gene does not indicate that each of the genes is associated with the same diseases. Meyer et al. (PG Pub 2003/0092019), for example, teaches that SNPs in the CADPKL gene are not each associated with neuropsychiatric disorders such as schizophrenia. Specifically Meyer teaches that cadpkl5 and cadpkl6 are not associated with the disease, however cadpkl7 has a p-value of less than 0.05, therefore an association exists (see table 5). Each of these polymorphisms are SNPs within the CADPKL gene, however, it is apparent that they are not all associated in the same manner with disease. Thus, Meyer exemplifies

that the association of a single SNP in a gene does not indicate that all SNPs within the gene are associated with the disease.

The level of skill in the art:

The level of skill in the art is deemed to be high.

Quantity of experimentation necessary:

In order to practice the invention as claimed, one would first have to establish that a predicative relationship exists between "any" variations in "any" ACTN3 gene and athletic performance in "any" mammal. Experimentation would be replete with unpredictable trial and error analysis because the specification teaches an ACTN# gene has not been found in all mammals, specifically horses. Further, Mills et al teaches that ACTN3 is not found in all mammals and the ACTN3 gene appears to have different expression patterns and function in mice relative to humans. Mills further teaches this R577X mutation has only been found in humans and occurred after the divergence of humans and primates from other mammals. Genecard teaches ACTN3 homologs have been identified in dogs, but not camel or horse. Further the specification and claims further limit individual to horse, dog, or camel. Thus the skilled artisan would have to determine if the ACTN3 gene is present in "any" mammal to be screened and further determine if there is one or more genetic variations in "any" mammal, then determine if the variations found result in altered performance. As the claims are drawn to "any" mammal the skilled artisan would have to determine which of the 4600 species have an ACTN3 gene. Then the artisan would have to determine if the ACTN3 gene or homologue has the same function as the human ACTN3 gene. This would further

require undue trial and error experimentation as Brenner teaches that different genes and homologs have different functions in different species, as Brenners teachings on leptin affecting obesity in mice, but not humans. This would require undue experimentation to isolate the gene, determine what a variation in the gene is, determine if the genes have the same function in the species examined, and correlate the variation to athletic performance.

The skilled artisan would further have to determine if "any" variation in ACTN3 results in altered athletic performance. This would be replete with trial and error experimentation because the art and the specification teach only examines the relationship of the R577X mutation and athletic performance. The art and specification are silent as to the effect of the other 8 known ACTN3 SNPs, as well as the effect of the 33 known 33ACTN3 cDNAs on athletic performance. Further the claims broadly encompass any mutation in any of the 16,406 nucleotides of the human ACTN3 gene as well as any mutation in any other mammalian ACTN3 gene. The specification or art do not teach or suggest that any mutation other the R577X mutation is predictably associated with athletic performance.

Further Meyer et al teaches that mutations in the same gene do not result in the same disease or phenotype of improved performance. Thus it would be unpredictable to associate "any" known or unknown variation in a single gene with a phenotype, even when there is the suggestion that a specific variation may play a role in that phenotype.

The skilled artisan would further have to determine what is encompassed by "any" ACTN3 gene. This would be replete with trial and error experimentation because

the ACTN3 gene has not been identified in every mammalian as previously discussed. Further, the ACTN3 has not been identified in 2 of the 4 species claimed. It would thus be unpredictable to associate "any" variations in "any" ACTN3 gene with a phenotype, when the gene has not been identified. This would be further unpredictable in light of the teachings of Brenner that the same gene (leptin) in different mammalian species undergo different evoluntionary pressures and thus result in different gene functions.

The skilled artisan would further have to determine if 577RR, 577RX, or 577XX are associated with altered or improved endurance, strength, sprint or power performance. The specification teaches that all 3 genotypes were found at similar levels in control and elite athletes. As the control population had the same genotypes as the elite athletes the specification teaches genotype is not associated with improved performance. The specification teaches when the elite athletes are divided into sprint athletes and endurance athletes, the male and female sprint athletes significantly different allele frequencies than controls. However, Moran et al found that R577X ACTN3 was positively correlated with sprint performance in males, but not other power specific tests and not at all in females. Thus it would be unpredictable to associate variations in R577X in strength, power, or endurance performance in view of the teachings of Moran, as the art and the specification have different findings with respect to "power" events and the effect on females and the specification teaches that controls and elite athletes have the same genotype. Though the specification and art appear to suggest a predictable correlation of the presence of the 577RR in males and sprint performance.

The skilled artisan would further have to determine if 577RR, 577RX, or 577XX are associated with altered or improved endurance performance. The specification teaches that the 577XX genotype was slightly higher in endurance athletes. However, Yang, Lucia, and Moran were not able to determine an effect of the 577XX allele in endurance performance of elite runners, elite cyclists, or adolescent children. Therefore it would be unpredictable to use a trend toward significance observed in the specification to associate with improved endurance performance when the post-filing art teaches these findings are unpredictable.

Due to the scope of the claims, one of skill in the art would be required to further undertake extensive trial and error experimentation to determine which mammals possess "any" genetic variation in "any" ACTN3 gene and determine if any found variations would result in improved athletic performance. However the claims do appear to be enabling for a method of determining sprint performance in human males comprising: obtaining a sample from a human male, analyzing the sample for the presence of the human ACTN3 577RR genotype, wherein the presence of the homozygous ACTN3 577R genotype is indicative of the possibility of improved sprint performance in human males

Therefore, in light of the breadth of the claims, the lack of guidance in the specification, the high level of unpredictability in the associated technology, the nature of the invention, the negative teachings in the art, and the quantity of unpredictable experimentation necessary to practice the claimed invention, it would require undue experimentation to practice the invention as claimed.

Response to arguments

The response asserts that the instant specification is enabling for the breadth of the claimed invention.

The response asserts that the teachings of Mills and paragraphs 32-40 of the instant specification are enabling for analyzing sprint performance, endurance performance, or strength performance in an individual other than human. These arguments have been thoroughly reviewed but are not considered persuasive because the cited paragraphs merely teach that the ACTN3 gene has been found in chimpanzees and baboons (paragraph 0033). Paragraph 38 teaches specifically, "although the equivalent gene has not yet been identified in horses, it is highly probable that a gene like ACTN3 exists in horses but has eluded detection." Thus the specification suggests that the ACTN3 gene may be present in other mammals, but does not provide support that any mutations or even the specific 577RR, 577RX or 577XX alleles are correlated in any mammal with any measure of athletic performance. The cited paragraphs merely speculate that such a relationship may exists. Additionally there is no evidence of record where the sequence of the gene in various mammals would be the same length and therefore an artisan would not know if the 577RR genotype will be the same nucleotide in each mammal. Such speculation is not evidence of enablement.

The response further asserts that Gene card teaches ACTN3 homologs have not been found in only 2 mammalian species of the 32 species recited in Gene Card, but 4 other species including the dog, mouse, chimpanzee and rat have been found. This

argument has been thoroughly been reviewed but is not considered persuasive because the specification specifically teaches the ACTN3 gene of horses has not been found; although the specification speculates mutations of the ACTN3 gene in horses as a predictor of performance has been claimed. Further as O'Brein teaches there are nearly 4600 mammalian species. Thus the fact a gene has been found in 5 mammalian species does not in any way indicated that these 5 species are representative of the entire genus of 4600 species. Further in view of the teaching of Brenner and Mills the presence of the ACTN3 gene in any other species does not suggest the same gene has the same function or expression pattern in different species that have undergone different selective pressures.

The response further asserts that the applicant has rejected the assertion that Yang et al as the sample size of Yang is too small as only 10% of the Ethiopians tested had the XX genotype and only 1% of the Kenyans had the XX genotype. The position is in direct contradiction to the conclusion of Yang, " This polymorphism does not contribute to the phenomenal success of the elite East African endurance runners" Last sentence of abstract). This appears to be argument that has not been supported by evidence.

As stated in the MPEP, 2106 "Arguments of Counsel"

"However, it must be emphasized that arguments of counsel alone cannot take the place of evidence in the record once an examiner has advanced a reasonable basis for questioning the disclosure. See In re Budnick, 537 F.2d at 538, 190 USPQ at 424; In re Schulze, 346 F.2d 600, 145 USPQ 716 (CCPA 1965); In re Cole, 326 F.2d 769, 140 USPQ 230 (CCPA 1964). For example, in a case where the record consisted substantially of arguments and opinions of applicant's attorney, the court indicated that factual affidavits could have provided important evidence on the issue of enablement."

This should not be construed as an invitation for providing evidence. As further stated in the MPEP 716.01 regarding the timely submission of evidence:

A) Timeliness.
Evidence traversing rejections must be timely or seasonably filed to be entered and entitled to consideration. In re Rothermel, 276 F.2d 393, 125 USPQ 328 (CCPA 1960). Affidavits and declarations submitted under 37 CFR 1.132 and other evidence traversing rejections are considered timely if submitted:
(1) prior to a final rejection,
(2) before appeal in an application not having a final rejection, or
(3) after final rejection and submitted
(i) with a first reply after final rejection for the purpose of overcoming a new ground of rejection or requirement made in the final rejection, or
(ii) with a satisfactory showing under 37 CFR 1.116(b) or 37 CFR 1.195, or
(iii) under 37 CFR 1.129(a).

Further the sample size of Yang is on the same order as the instant specification, thus the arguments of sample size suggest the allelic frequency is ethnicity dependent. Thus the instant specification is not enabling for all races or ethnic groups.

The response further asserts that the Applicant disagrees with the teachings of Moran. Once again it is noted that the response is disagreeing with the conclusion of the art of Moran teaches, "We found no evidence that the R577X genotype is associated with endurance or obesity related genotypes" (see page 93, 1st column last paragraph). Once again the response is presenting arguments that are not supported by evidence.

The response continues to assert that Moran does not "show results following suitable training regimes to be able to draw such a conclusion" (last paragraph page 15 of response). This argument has been thoroughly reviewed but is not considered

persuasive as the claims, nor the specification require or suggest that the training regime of an mammal is to be considered in determining athletic performance. Thus this argument appears to suggest that physical training regimes in addition to the genotyping are required the determination of athletic performance, which is a feature that is not claimed.

The response on the top of page 16 further continues to suggest more appropriate test for maximizing sprint potential than those presented by Moran. These arguments have been reviewed but are not considered persuasive because the claims and specification are drawn to the determination of athletic performance solely based on genotype of the ACTN3 gene. These arguments appear to suggest that a step of training of the individuals is required, however this step is suggested by the specification or claimed. Thus these arguments appear to suggest that the claims are not enabled for any non trained individual.

The response further points out that the specification, and apparently the claims, are drawn to a comparison of elite athletes and suitable controls, not the non-elite adolescents of Moran. This once again appears to suggest that the training an/or the population studied is a major factor in determining the predictability of the claimed invention. Further this argument is directed to elements not present in the instant claims and thus is moot.

The response further asserts that due to the a small sample size the teachings of Lucia and invalid and quotes page 883 where Lucia addresses the limitations of his studies. It is noted that there are limitations of Lucia studies, but in combination with the

teachings of Yang and Moran it definitely suggests that mutation Is not predictably associated with endurance performance. The response omitted that Lucia address the limitation of the study is the lack of inclusion of female athletes, as the ACTN3 577XX mutation may have a greater affect on females that males. This limitation is directly contradicted by the teachings of Moran, and further strengthens the argument for the unpredictability of the claimed invention in human females.

The response asserts that the teachings of Niemi et al attached in appendix A supports their arguments. This argument has been thoroughly reviewed but the reference of Neimi has a small sample size of athletes (141) and only 2 sprint athletes total that have the X allele (see table 2). Neimi teaches 120 Finish blood donors were used as controls. Thus according to applicants arguments against Yang it would be unpredictable to associate the findings of such a small sample size with so few athletes that were homozygous to either R577X allele to have proper statistical power to make any conclusions. Thus the argument does not meet the standards set forth earlier in the response. At best this suggest the results are unpredictable in light of all other art of record.

The response further asserts that the teachings of Papadimitrou et al confirms applicants finding with respect to power athletes. This arguments has been thoroughly reviewed but is not considered persuasive Papadimitrou as with Neimi and Yang have a small sample size of 101 total elite athletes. Although Papadimitrou appears to confirm the teachings complete analysis of Papadimitrou reference is not possible as a paragraph on the next to last page has been blacked out. However, Papadimitrou

teaches that the ACTN3 gene is less important in endurance events as the RR and XX genotype have been found in many Olympic endurance athletes (see next to lat page, last paragraph). Thus the argument does not meet the standards set forth earlier in the response. At best this suggest the results are unpredictable in light of all other art of record.

The response further presents an abstract from Roth and assert the XX genotype is negatively correlated with strength athletes. This argument has been thoroughly reviewed but the reference of Roth has a small sample size of strength athletes (79). Roth thus appears to suggest that the XX allele is underrepresented in strength athletes, but provides no evidence of a predictable relationship with endurance.

The response further presents the teachings of MacArthur et al (Nature Genetics 2007 (39, pages 1261-1265) and asserts the teachings of MacArthur enable the endurance correlation of 577XX with endurance by use of transgenic mice. This argument has been thoroughly reviewed but is not persuasive for the enablement of the endurance in any mammal. As Mills teaches that ACTN3 has different expression patterns and potentially function in mice and humans. Mills specifically teaches that human muscle fibers have co-expression of ACTN2 and ACTN3, while mice fibers can have ACTN2 or ACTN3 or both. Thus suggesting ACTN3 have different regulation and function in mice and humans. When these teachings are taken in further light of Brenner's teaching that homologous genes have different functions in different species due to different selective pressures, it would be unpredictable to extrapolate the findings

in a single study in mice to "any" mammal in that the expression of ACTN3 is different across species.

Thus this rejection has been maintained. While the specification appears to be enabling for a method of determining sprint performance in human males comprising: obtaining a sample from a human male, analyzing the sample for the presence of the human ACTN3 577RR genotype, wherein the presence of the homozygous ACTN3 577R genotype is indicative of the possibility of improved sprint performance, strength or power in human males does not reasonably provide enablement for predicting sprint performance, endurance performance, power performance, or strength performance in any male or any female in any mammalian species by the detection any variation in the ACTN3 gene.

3. Claims 1, 3-16, 18, 24-40 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejected claims 1-16, 18, 24-38 encompass "any" variation in "any" ACTN3 in "any" mammalian species. Claim 2 does draw this to human ACTN3, while claim 3 draws to horse, camel, or dog ACTN3. The claims do not set forth any structural requirements for ACTN3.

When the claims are analyzed in light of the specification, the invention encompasses an enormous number of nucleotide molecules. The specification teaches a nucleic acid is from 1 nucleotide up to the whole chromosome. Thus the recitation of ACTN3 encompasses any nucleic acid or any nucleic acid variation on chromosome 11. Further the claims encompass any nucleic acid that can broadly be identified as ACTN3 in any of the 4600 to 4800 mammalian species (Science magazine (1999) volume 286, pages 458-481)(see page 458, 1st column 2nd paragraph).

In analyzing whether the written description requirement is met for genus claims, it is first determined whether a representative number of species have been disclosed. The instant specification does not teach the sequence of "any" ACTN3 gene in humans or "any" mammal. The specification teaches that, " it is highly probable that a gene like ACTN3 exists in horses but has eluded detection" (see paragraph 0038). The specification thus teaches that applicant did not possess the horse ACTN3 at the time invention was made. Similarly, dog and camel ACTN3 were not taught or described in the specification. Thus the specification does not teach a single species of the ACTN3 gene.

Next, it is determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics (e.g. other nucleotide sequences or positions with in a specific gene or nucleic acid), specific features and functional attributes that would distinguish different members of the claimed genus. In the instant case the specification provides no structural or functional limitation for ACTN3 gene or variations in the ACTN3. The claims read in light of the specification

encompass any nucleic acid molecule that is present on the same chromosome as ACTN3 or has homology with ACTN3 in any mammalian species. Further, the claims are drawn to any variation in the ACTN3 gene or the chromosome, which it is on. This is an enormous genus of nucleic acids.

Gene card (genecards.org/cgi-bin/carddisp.pl?gene=ACTN3&search=actn3&suff=txt, pages 1-11, 3/24/2007) teaches ACTN3 homologs have only been found in dog, fruitfly, zebrafish, mouse, chimpanzee, and rat (see page 11), while listing 32 species in which a homolog of ACTN3 has not been found. Genecard teaches there are 16,406 bases in the ACTN3 gene. Genecard further teaches there are 9 known SNPs in the human ACTN3 gene and 33 cDNAs. Thus Genecard teaches the recitation of "any" variation of ACTN3 boradly encompasses an enormous genus of nucleic acids, as it encompasses any ACTN3 gene or any mutation in any nucleotide or multiple nucleotides that comprise the 16,406 nucleotides of human ACTN3.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

The skilled artisan cannot envision the detailed chemical structure of the encompassed ACTN3 gene and variations regardless of the complexity or simplicity of

the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993), and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. The current situation is a definition of the compound solely based on its functional utility, as a polymorphism, without any definition of the particular polymorphisms claimed.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

In the instant application, the provided information regarding nucleic acid ACTN3 or any variations, do not constitute an adequate written description of the broad subject matter of the claims, and so one of skill in the art cannot envision the detailed chemical structure of the nucleic acids encompassed by the ACTN3 gene. The claims require “any” genetic variations. The art accepts genetic variations to include transversions, insertions, deletions, translocation, substitutions, and rearrangements. The

specification does not describe any insertions, deletions, translocation, substitutions, and rearrangements. Thus the specification does not teach a representative number of species from this enormous genus. Adequate written description requires more than a statement that nucleic acids with a particular quality are part of the invention and reference to a potential method for their identification. The nucleic acid sequence is required.

In conclusion, the limited information provided regarding the 577X variation in the human ACTN3 is not deemed sufficient to reasonably convey to one skilled in the art nucleic acid molecules encompassed by "any" genetic variation in "any" mammalian ACTN3.

Thus, having considered the breadth of the claims and the provisions of the specification, it is concluded that the specification does not provide adequate written description for the claims.

Summary

No claims are allowed.

Conclusions

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Steven C. Pohnert whose telephone number is 571-272-3803. The examiner can normally be reached on Monday-Friday 7:00-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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